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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
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1629	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/762,566	FRANKLIN, RICHARD	
	Examiner	Art Unit	
	Leslie A. Royds Draper	1629	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 November 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2,12,13 and 17-22* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2,12-13,17-22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *29Jul10;07Mar11*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 2, 12-13 and 17-22 are presented for examination.

In view of the Appeal Brief filed on November 5, 2010, **PROSECUTION IS HEREBY REOPENED**. New grounds of rejection are set forth below.

To avoid abandonment of the application, Appellant must exercise one of the following two options:

(1) file a reply under 37 CFR 1.111 (if this Office action is non-final) or a reply under 37 CFR 1.113 (if this Office action is final); or,

(2) initiate a new appeal by filing a notice of appeal under 37 CFR 41.31 followed by an appeal brief under 37 CFR 41.37. The previously paid notice of appeal fee and appeal brief fee can be applied to the new appeal. If, however, the appeal fees set forth in 37 CFR 41.20 have been increased since they were previously paid, then Appellant must pay the difference between the increased fees and the amount previously paid.

A Supervisory Patent Examiner (SPE) has approved of reopening prosecution by signing below:

Claims 2, 12-13 and 17-22 remain pending and under examination.

Applicant's Information Disclosure Statements (IDS) filed July 29, 2010 (two pages) and March 7, 2011 (two pages) have each been received and entered into the present application. As reflected by the attached, completed copies of form PTO/SB/08a (four pages total), the Examiner has considered the cited references.

Applicant's arguments, presented in the Appeal Brief filed November 5, 2010, have been fully considered. Rejections and/or objections not reiterated from the final Office Action are hereby withdrawn.

The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set of rejections and/or objections presently being applied to the instant application.

Claim Rejections - 35 USC § 112, Second Paragraph (New Grounds of Rejection)

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 20 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention.

The limitation of "said system comprises at least two distinct layers comprising the anagrelide or anagrelide salt and at least one adhesive, and a single backing film" renders the claim indefinite because the composition of each of the two layers is not clearly, precisely or deliberately set forth in the claims. It is unclear if the two distinct layers are (1) the anagrelide or anagrelide salt and (2) at least one adhesive, and further wherein the system additionally comprises a single backing film, or if the two distinct layers are (1) the anagrelide or anagrelide salt with at least one adhesive and (2) a single backing film. The construction of the layers is not clearly defined in the claim as presently written such that one of ordinary skill in the art at the time of the invention would have been reasonably apprised of the metes and bounds of the subject matter for which Applicant is presently seeking protection. Clarification is required.

For these reasons, the claim fails to meet the tenor and express requirements of 35 U.S.C. 112, second paragraph, and is, thus, properly rejected.

Claim 22 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention.

Present claim 22 is directed to administering anagrelide or an anagrelide salt via a transdermal patch having a matrix system comprising a semisolid matrix containing a solution or suspension of the

anagrelide or anagrelide salt which is in direct contact with a release liner, and a skin adhesion component incorporated in an overlay which forms a concentric configuration around said semisolid matrix.

The limitation of the "skin adhesion component incorporated in an overlay which forms a concentric configuration around said semisolid matrix" renders the claim indefinite because the configuration of the skin adhesion component in relation to the other components of the transdermal patch is not clearly, precisely or deliberately set forth. The claim stipulates that the semisolid matrix (which contains the solution or suspension of the anagrelide or salt thereof) is in direct contact with a release liner. However, the claim further states that the skin adhesion component overlays the semisolid matrix and envelopes the matrix (i.e., understood to be specified by the limitation "concentric configuration"), but it is unclear how the skin adhesion component can directly overlay the matrix per se if the matrix must be in direct contact with a release liner. As a result, the exact configuration of the patch is not clearly described in the claim because it is unclear if the patch comprises (1) a semisolid matrix, covered by a release liner and overlayed with a skin adhesion component or (2) a semisolid matrix overlayed with a skin adhesion component, which is covered by a release liner. Due to this ambiguity of the claim, one of ordinary skill in the art at the time of the invention would not have been reasonably apprised of the metes and bounds of the subject matter for which Applicant is presently seeking protection. Clarification is required.

For these reasons, the claim fails to meet the tenor and express requirements of 35 U.S.C. 112, second paragraph, and is, thus, properly rejected.

Claim Rejections - 35 USC § 103 (New Grounds of Rejection)

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person

having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 2, 12-13 and 17-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Anagrelide Study Group ("Anagrelide, a Therapy for Thrombocythemic States: Experience in 577 Patients", Am J Med, 1992; 92(1):69-76; herein after "Anagrelide SG") in view of Hanson (U.S. Patent No. 6.585,995; 2003, cited by Applicant) and Mitchel et al. ("Transdermal Drug Delivery-Clinical and Regulatory Strategies", American Academy of Dermatology Annual Meeting, March 2000; Abstract), and further in view of Barnhart et al. (U.S. Patent No. 5,762,952; 1998).

Anagrelide SG teaches the treatment of 577 patients with anagrelide to control thrombocytosis of chronic myeloproliferative diseases (abstract), wherein 335 patients had primary thrombocythemia, 114 had chronic granulocytic leukemia, 68 had polycythemia vera and 60 had undifferentiated myeloproliferative diseases (abstract). Anagrelide SG teaches that thrombocytosis occurs in a variety of clinical settings with chronic elevations of platelet numbers observed in myeloproliferative diseases, including polycythemia vera, chronic granulocytic leukemia and essential thrombocythemia (col.1, para.1, l.69). Anagrelide SG teaches that the compound anagrelide inhibits cyclic nucleotide phosphodiesterase and the release of arachidonic acid from phospholipase and inhibits platelet aggregation (col.2, para.2, p.69). Anagrelide SG teaches that the average dose effective to control platelets was determined to be between 2.0 and 2.5 mg/day (col.1, para.5, p.70). Anagrelide SG confirms that anagrelide is effective for reducing platelet counts in over 90% of patients evaluable for response whether or not they have been previously treated, regardless of the prior therapy used or response to that therapy (col.1, para.3, p.75), and that the extensive experience with anagrelide demonstrates that it can be used safely and effectively to treat patients with thrombocythemia of various origins (col.1, para.3, p.76).

Anagrelide SG fails to teach (1) transdermal administration of anagrelide in an amount of 0.1-20 mg/kg/day (claims 1 and 13), wherein the transdermal administration minimizes first pass liver metabolism thereby reducing the plasma concentration of 3-hydroxy anagrelide compared to a patient

orally administered the equivalent amount of anagrelide (claim 2) and (2) wherein the anagrelide further comprises a skin permeation enhancer (claim 18) and is in a transdermal patch of the types described in instant claims 19-20.

Hanson et al. teaches therapeutic methods of inhibiting vasoocclusive events by administering agents that reduce the number of circulating platelets to below normal levels (abstract), wherein the preferred agent to be administered is anagrelide (col.3, l.66), which is effective to reduce platelets in a dosage ranging from 1 μg/kg/day to 10 mg/kg/day, preferably from 1 μg/kg/day to 150 μg/kg/day or from 30 μg/kg/day to 150 μg/kg/day (col.17, l.65-col.18, l.9), and further wherein the agent is administered in a manner effective to provide the active agent without causing clinically unacceptable adverse events, such as, inter alia, transdermal administration (col.18, l.10-18).

One of ordinary skill in the art at the time of the invention would have found it prima facie obvious to administer anagrelide to a patient suffering from thrombocythemia of various origin (e.g., polycythemia vera, etc.) as disclosed in Anagrelide SG transdermally because transdermal administration of anagrelide was known to be an effective route of administration of the compound for the purpose of reducing platelet counts in a patient in need thereof without causing clinically unacceptable toxicity, as evidenced by Hanson et al. One of ordinary skill in the art at the time of the invention would have further found it prima facie obvious to administer anagrelide to a human subject for the treatment of thrombocythemia and would, therefore, modify the dosage disclosed in Anagrelide SG to be a therapeutic dosage appropriate for the subject to be treated such that the skilled artisan would have had a reasonable expectation that the dose of anagrelide to be administered to a human subject in need thereof would have been sufficient to elicit the therapeutic effect of the compound. Specifically, one of skill in the art would have been motivated to employ the dosage range, e.g., 1 μg/kg/day to 10 mg/kg/day, as disclosed by Hanson et al., to function to reduce the number of circulating platelets in a human subject in need of such reduction. Such a person would have had a reasonable expectation of successfully treating

thrombocythemia in a human subject using anagrelide in a dosage amount of, e.g., 1 μg/kg/day to 10 mg/kg/day, as evidenced by Hanson et al. to be an amount effective to achieve the reduction in the number of circulating platelets.

Note also that the determination of the optimal dosage amount would have been a matter well within the skill of the artisan at the time of the invention and would not have required undue experimentation or have been outside the realm of knowledge generally available to the skilled artisan. Factors that would have been taken into consideration when making such a determination would have included, but not been limited to, the age, body weight, symptoms, desired therapeutic effect, route of administration, duration of treatment, etc. Other factors that would have been considered would have included the sex, diet and medical condition of the patient, severity of the disease, pharmacological considerations, e.g., activity, efficacy, pharmacokinetics and toxicology profiles of the particular compound employed, whether a drug delivery system is utilized and whether the compound is administered as part of a drug combination. Thus, the dosage amount of anagrelide that would have actually been employed would have been expected to vary widely and, in the absence of evidence to the contrary, would not have been inconsistent with that which is presently claimed, absent factual evidence to the contrary.

Mitchel et al. teaches that transdermal delivery of a drug product allows for the avoidance of first pass metabolism by the liver as compared to an oral dosage form of the same product and the delivery of a more even level of the therapeutic agent over the course of 24 hours (abstract). Mitchel et al. further teaches that the most common form of transdermal delivery is by using a dermal patch (abstract).

One of ordinary skill in the art at the time of the invention would have found it prima facie obvious to employ transdermal administration, such as in the form of a dermal patch, as the mode of administration of anagrelide because, as evidenced by Hanson et al., anagrelide is amenable to formulation for transdermal administration, and as further evidenced by Mitchel et al., transdermal

delivery permits the avoidance of first pass metabolism by the liver, which can result in unwanted side effects as a result of the metabolism. Such a person would have been further motivated to do so in view of the fact that it was well known in the art that transdermal delivery permits a more even level of the therapeutic agent over the course of 24 hours, as evidenced by Mitchel et al.

Regarding Applicant's instantly claimed property of claim 2, i.e., that transdermal administration minimizes first pass liver metabolism thereby reducing the plasma concentration of 3-hydroxyanagrelide compared to a patient orally administered the equivalent amount of anagrelide, Mitchel et al. provides the clear evidence that transdermal administration of the claimed active agent anagrelide would have necessarily resulted in minimized first pass liver metabolism because this is an inherent function of transdermal applications. Though the property of "reducing the plasma concentration of 3-hydroxyanagrelide compared to a patient orally administered the equivalent amount of anagrelide" is not specifically disclosed by the cited prior art references, the compound and method steps as disclosed by Anagrelide SG in view of Hanson et al. and Mitchel et al. are identical to that instantly claimed. Therefore, this property of minimizing "first pass liver metabolism thereby reducing the plasma concentration of 3-hydroxyanagrelide compared to a patient orally administered the equivalent amount of anagrelide" must necessarily be disclosed in the method described by the cited prior art because products of identical chemical composition cannot exert mutually exclusive properties when used in the same manner under the same circumstances. If the prior art teaches the identical chemical or physical structure of the compound (i.e., same active agent, same physical structure, same effective amount, etc.) and the compound is used in the same manner (i.e., administered in the same manner to the same host subject), the properties that Applicant discloses and/or claims must necessarily be present. MPEP §2112.

In re Best (195 USPQ 430) and In re Fitzgerald (205 USPQ 594) discuss the support of rejections wherein the prior art discloses subject matter, which there is reason to believe necessarily includes functions that are newly cited, or is identical to a product instantly claimed. In such a situation, the burden

is shifted to the Applicants to "prove that the subject matter to be shown in the prior art does not possess the characteristic relied on" (205 USPQ 592, second column, first full paragraph). There is no requirement that a person of ordinary skill in the art would have recognized this necessarily present disclosure at the time of the invention, but only that the subject matter is, in fact, necessarily present in the prior art reference. Schering Corp. v. Geneva Pharm. Inc., 339 F.3d 1373, 1377, 67 USPQ2d 1664, 1668 (Fed. Cir. 2003); see also Toro Co. v. Deere & Co., 355 F.3d 1313, 1320, 69 USPQ2d 1584, 1590 (Fed. Cir. 2004) ("IT]he fact that a characteristic is a necessary feature or result of a prior-art embodiment (that is itself sufficiently described and enabled) is enough for inherent anticipation, even if that fact was unknown at the time of the prior invention"). Note that, even though Toro was decided in the context of inherent anticipation, considerations of inherent teachings arise both in the context of anticipation and obviousness (see, e.g., In re Napier, 55 F.3d 610, 613, 34 USPQ2d 1782, 1784 (Fed. Cir. 1995) or In re Grasselli, 713 F.2d 731,739, 218 USPQ 769, 775 (Fed. Cir. 1983) and MPEP §2112). The burden is now shifted to Applicant to prove that, in fact, the prior art method does not possess this same characteristic as now claimed.

Barnhart et al. teaches a transdermal delivery system for delivery of an active drug (col.1, l.6-8), wherein the system comprises a backing layer having coated thereon an active drug-containing adhesive layer that includes (a) an acrylic-based adhesive that is self-crosslinking at a temperature of from about 20°C to about 65°C and (b) an active drug (i.e., which meets Applicant's requirement of a two layer transdermal patch comprising anagrelide with an adhesive in one layer and a backing film in another layer as recited in instant claim 20; abstract), wherein the active drug is mixed with the acrylic adhesive solution to form an active drug-adhesive mixture (abstract). Barnhart et al. further teaches that a skin permeation enhancer may be further included in the drug mixture and include, inter alia, oleic acid (i.e., which meets Applicant's requirement of a drug-in-adhesive composition that contains anagrelide and a permeation enhancer as an excipient and an adhesive, combined with a backing layer as recited in instant

claim 19; col.6, l.24-32). Barnhart et al. teaches that the disclosed patch does not cause a high incidence of human allergic responses, such as contact dermatitis (col.2, l.64-67).

One of ordinary skill in the art at the time of the invention would have found it prima facie obvious to incorporate anagrelide into the transdermal patch delivery system of Barnhart et al. (which, notably, is disclosed to be functional to retain any type of active drug), which provides for an effective dermal patch for transdermal administration of an active drug to a patient in need thereof. Such a person would have been motivated to do so in order to effectively administer the agent transdermally to effective an even level of distribution of the therapeutic agent (see Mitchel et al.) and also to provide the drug in a patch that provides efficient administration while reducing allergic responses to the dermal patch and adhesives therein, as evidenced by the disclosure of Barnhart et al.

Claims 2, 12-13, 17 and 21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Anagrelide Study Group ("Anagrelide, a Therapy for Thrombocythemic States: Experience in 577 Patients", Am J Med, 1992; 92(1):69-76; herein after "Anagrelide SG") in view of Hanson (U.S. Patent No. 6.585,995; 2003, cited by Applicant) and Mitchel et al. ("Transdermal Drug Delivery-Clinical and Regulatory Strategies", American Academy of Dermatology Annual Meeting, March 2000; Abstract), and further in view of Zupon et al. (EP 0252459; 1987).

Anagrelide SG teaches the treatment of 577 patients with anagrelide to control thrombocytosis of chronic myeloproliferative diseases (abstract), wherein 335 patients had primary thrombocythemia, 114 had chronic granulocytic leukemia, 68 had polycythemia vera and 60 had undifferentiated myeloproliferative diseases (abstract). Anagrelide SG teaches that thrombocytosis occurs in a variety of clinical settings with chronic elevations of platelet numbers observed in myeloproliferative diseases, including polycythemia vera, chronic granulocytic leukemia and essential thrombocythemia (col.1, para.1, l.69). Anagrelide SG teaches that the compound anagrelide inhibits cyclic nucleotide

phosphodiesterase and the release of arachidonic acid from phospholipase and inhibits platelet aggregation (col.2, para.2, p.69). Anagrelide SG teaches that the average dose effective to control platelets was determined to be between 2.0 and 2.5 mg/day (col.1, para.5, p.70). Anagrelide SG confirms that anagrelide is effective for reducing platelet counts in over 90% of patients evaluable for response whether or not they have been previously treated, regardless of the prior therapy used or response to that therapy (col.1, para.3, p.75), and that the extensive experience with anagrelide demonstrates that it can be used safely and effectively to treat patients with thrombocythemia (col.1, para.3. p.76).

Anagrelide SG fails to teach (1) transdermal administration of anagrelide in an amount of 0.1-20 mg/kg/day (claims 1 and 13), wherein the transdermal administration minimizes first pass liver metabolism, thereby reducing the plasma concentration of 3-hydroxy anagrelide compared to a patient orally administered the equivalent amount of anagrelide (claim 2) and (2) wherein the anagrelide is in a transdermal patch of the type described in instant claim 21.

Hanson et al. teaches therapeutic methods of inhibiting vasoocclusive events by administering agents that reduce the number of circulating platelets to below normal levels (abstract), wherein the preferred agent to be administered is anagrelide (col.3, l.66), which is effective to reduce platelets in a dosage ranging from 1 μg/kg/day to 10 mg/kg/day, preferably from 1 μg/kg/day to 150 μg/kg/day or from 30 μg/kg/day to 150 μg/kg/day (col.17, l.65-col.18, l.9), and further wherein the agent is administered in a manner effective to provide the active agent without causing clinically unacceptable adverse events, inter alia, transdermal administration (col.18, l.10-18).

One of ordinary skill in the art at the time of the invention would have found it prima facie obvious to administer anagrelide to a patient suffering from thrombocythemia of various origin (e.g., polycythemia vera, etc.) as disclosed in Anagrelide SG transdermally because transdermal administration of anagrelide was known to be an effective route of administration of the compound for the purpose of reducing platelet counts in a patient in need thereof without causing clinically unacceptable toxicity, as

evidenced by Hanson et al. One of ordinary skill in the art at the time of the invention would have further found it prima facie obvious to administer anagrelide to a human subject for the treatment of thrombocythemia and would, therefore, modify the dosage disclosed in Anagrelide SG to be a therapeutic dosage appropriate for the subject to be treated such that the skilled artisan would have had a reasonable expectation that the dose of anagrelide to be administered to a human subject in need thereof would have been sufficient to elicit the therapeutic effect of the compound. Specifically, one of skill in the art would have been motivated to employ the dosage range, e.g., 1 μg/kg/day to 10 mg/kg/day, as disclosed by Hanson et al. to function to reduce the number of circulating platelets, in a human subject in need of such reduction. Such a person would have had a reasonable expectation of successfully treating thrombocythemia in a human subject using anagrelide in a dosage amount of, e.g., 1 μg/kg/day to 10 mg/kg/day, as evidenced by Hanson et al. to be an amount effective to achieve the reduction in the number of circulating platelets.

Note also that the determination of the optimal dosage amount would have been a matter well within the skill of the artisan at the time of the invention and would not have required undue experimentation or have been outside the realm of knowledge generally available to the skilled artisan. Factors that would have been taken into consideration when making such a determination would have included, but not been limited to, the age, body weight, symptoms, desired therapeutic effect, route of administration, duration of treatment, etc. Other factors that would have been considered would have included the sex, diet and medical condition of the patient, severity of the disease, pharmacological considerations, e.g., activity, efficacy, pharmacokinetics and toxicology profiles of the particular compound employed, whether a drug delivery system is utilized and whether the compound is administered as part of a drug combination. Thus, the dosage amount of anagrelide that would have actually been employed would have been expected to vary widely and, in the absence of evidence to the

contrary, would not have been inconsistent with that which is presently claimed, absent factual evidence to the contrary.

Mitchel et al. teaches that transdermal delivery of a drug product allows for the avoidance of first pass metabolism by the liver as compared to an oral dosage form of the same product and the delivery of a more even level of the therapeutic agent over the course of 24 hours (abstract). Mitchel et al. further teaches that the most common form of transdermal delivery is by using a dermal patch (abstract).

One of ordinary skill in the art at the time of the invention would have found it prima facie obvious to employ transdermal administration, such as in the form of a dermal patch, as the mode of administration of anagrelide because, as evidenced by Hanson et al., anagrelide is amenable to formulation for transdermal administration, and as further evidenced by Mitchel et al., transdermal delivery permits the avoidance of first pass metabolism by the liver, which can result in unwanted side effects as a result of the metabolism. Such a person would have been further motivated to do so in view of the fact that it was well known in the art that transdermal delivery permits a more even level of the therapeutic agent over the course of 24 hours, as evidenced by Mitchel et al.

Regarding Applicant's instantly claimed property of claim 2, i.e., that transdermal administration minimizes first pass liver metabolism thereby reducing the plasma concentration of 3-hydroxyanagrelide compared to a patient orally administered the equivalent amount of anagrelide, Mitchel et al. provides the clear evidence that a transdermal administration of the claimed active agent anagrelide would have necessarily resulted in minimized first pass liver metabolism because this is an inherent function of transdermal applications. Though the property of "reducing the plasma concentration of 3-hydroxyanagrelide compared to a patient orally administered the equivalent amount of anagrelide" is not specifically disclosed by the cited prior art references, the compound and method steps as disclosed by Anagrelide SG in view of Hanson et al. and Mitchel et al. are identical to that instantly claimed. Therefore, this property of minimizing "first pass liver metabolism thereby reducing the plasma

concentration of 3-hydroxyanagrelide compared to a patient orally administered the equivalent amount of anagrelide" must necessarily be disclosed in the method described by the cited prior art because products of identical chemical composition cannot exert mutually exclusive properties when used in the same manner under the same circumstances. If the prior art teaches the identical chemical or physical structure of the compound (i.e., same active agent, same physical structure, same effective amount, etc.) and the compound is used in the same manner (i.e., administered in the same manner to the same host subject), the properties that Applicant discloses and/or claims must necessarily be present. MPEP §2112.

In re Best (195 USPQ 430) and In re Fitzgerald (205 USPQ 594) discuss the support of rejections wherein the prior art discloses subject matter, which there is reason to believe necessarily includes functions that are newly cited, or is identical to a product instantly claimed. In such a situation, the burden is shifted to the Applicants to "prove that the subject matter to be shown in the prior art does not possess the characteristic relied on" (205 USPQ 592, second column, first full paragraph). There is no requirement that a person of ordinary skill in the art would have recognized this necessarily present disclosure at the time of the invention, but only that the subject matter is, in fact, necessarily present in the prior art reference. Schering Corp. v. Geneva Pharm. Inc., 339 F.3d 1373, 1377, 67 USPQ2d 1664, 1668 (Fed. Cir. 2003); see also Toro Co. v. Deere & Co., 355 F.3d 1313, 1320, 69 USPQ2d 1584, 1590 (Fed. Cir. 2004) ("IT]he fact that a characteristic is a necessary feature or result of a prior-art embodiment (that is itself sufficiently described and enabled) is enough for inherent anticipation, even if that fact was unknown at the time of the prior invention"). Note that, even though Toro was decided in the context of inherent anticipation, considerations of inherent teachings arise both in the context of anticipation and obviousness (see, e.g., In re Napier, 55 F.3d 610, 613, 34 USPQ2d 1782, 1784 (Fed. Cir. 1995) or In re Grasselli, 713 F.2d 731,739, 218 USPQ 769, 775 (Fed. Cir. 1983) and MPEP §2112). The burden is now shifted to Applicant to prove that, in fact, the prior art method does not possess this same characteristic as now claimed.

Zupon et al. teaches that transdermal delivery devices are well known in the art as convenient and efficient means for controlled administration of drugs and typically comprise a backing layer defining one face surface, an adhesive layer defining the other face surface, wherein the adhesive layer is protected until use by a release liner, and between the face surfaces a drug reservoir layer confined within wall members (p.2, l.5-8). Zupon et al. further teaches that the drug reservoir usually has an upper wall member (i.e., the upper wall member is contiguous with the backing layer) and usually a lower wall member between the adhesive and the reservoir which may be a rate-controlling membrane (i.e., understood to be a semi-permeable membrane due to its rate controlling property), a non-rate controlling membrane or an impervious layer in which one or more wicks run between the reservoir and adhesive (p.2, l.8-12). Zupon et al. states that the reservoir may comprise a hollow container for holding liquid and the active drug may be present only in the reservoir (i.e., wherein the reservoir contains a solution of active drug) or also incorporated into the adhesive layer (p.2, l.12-14).

One of ordinary skill in the art at the time of the invention would have found it prima facie obvious to incorporate anagrelide into the transdermal patch delivery system, such as that of Zupon et al. (which, notably, is disclosed to be functional to retain any type of active drug), which provides for an effective dermal patch for transdermal administration of an active drug to a patient in need thereof. Such a person would have been motivated to do so in order to effectively administer the agent transdermally to effective an even level of distribution of the therapeutic agent (see Mitchel et al.) and also to provide the drug in a patch that provides an efficacious, convenient and efficient means for controlled administration of the active agent.

Conclusion

Rejection of claims 2, 12-13 and 17-22 is proper.

No claims of the present application are allowed.

Applicant is requested to specifically point out the support for any amendments made to the disclosure in response to this Office action, including the claims (MPEP §714.02 and §2163.06). In doing so, applicant is requested to refer to pages and line numbers in the as-filed specification, not the published application. Due to the procedure outlined in MPEP §2163.06 for interpreting claims, it is noted that other art may be applicable under 35 U.S.C. §102 or 35 U.S.C. §103(a) once the aforementioned issue(s) is/are addressed.

Applicant is requested to provide a list of all copending U.S. applications that set forth similar subject matter to the present claims and share an inventor or assignee with the instant application. A copy of such copending claims is requested in response to this Office action in order to assist the examiner with double patenting analysis in the application.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leslie A. Royds Draper whose telephone number is (571)-272-6096. The examiner can normally be reached on Monday-Friday (9:00 AM-5:30 PM).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey S. Lundgren can be reached on (571)-272-5541. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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April 21, 2011

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